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# TITLE: ACUTE TRUCAL ATAXIA WITHOUT NYSTAGMUS IN PATIENTS WITH ACUTE VERTIGO

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## ABSTRACT

Introduction: The acute vestibular syndrome (AVS) describes sudden-onset, continuous vertigo lasting >24 hours with associated nystagmus, nausea, and vomiting. Differentiating between peripheral and central aetiologies can be challenging in the acute phase given substantial symptom overlap. A detailed clinical history and focused physical eye movement examination such as the HINTS eye examination has been purported to be the most reliable approach to identify acute cerebellar/brainstem stroke, outperforming even acute brain imaging. We have observed, however, that isolated vertigo may be accompanied by acute truncal ataxia, in the absence of nystagmus.

Methods: We explored the frequency of ataxia without concurrent nystagmus in a cross-section of patients with acute vertigo who presented to the emergency department at two centres in Argentina (Group A) and United Kingdom (Group B). Patients underwent detailed clinical neuro-otological assessments (Groups A & B), that included instrumented head impulse testing and oculography (Group B).

Results: A total of 71 patients in Group A and 24 patients in Group B were included in this study. We found acute truncal ataxia – without nystagmus - in 15% (n=14) of our cohort. Lesions involved stroke syndromes affecting the posterior inferior cerebellar artery, anterior inferior cerebellar artery, superior cerebellar artery, thalamic stroke, cerebral stroke (middle cerebral artery), multiple sclerosis, and cerebellar tumour. Additional eye movement assessment was normal in these individuals, even with oculography.

Conclusions: We have identified a significant subpopulation of patients with acute vertigo in which the current standard approaches such as the HINTS examination that focus on oculomotor assessment may not be applicable, highlighting the need for a formal assessment of gait this setting.

# INTRODUCTION

The acute vestibular syndrome (AVS) is defined as sudden-onset, continuous vertigo lasting >24 hours with associated nystagmus, nausea, and vomiting, all of which are worsened with head movement (1).

Differentiating between peripheral and central aetiologies can be challenging in the acute phase. In addition, recent studies highlight the presence of false negative 'gold standard' MRI scans in posterior circulation strokes, in the first 48 hours following symptom onset (2). In fact, a focused physical eye movement examination may be the most reliable approach to identify acute cerebellar stroke, namely HINTS*plus* (horizontal Head Impulse test, Nystagmus and Test of Skew *plus* a bedside test of hearing), identifying stroke with a sensitivity and specificity approaching 100% in patients with AVS (2), albeit when conducted by experts (3).

Severe difficulty or inability to stand is another core feature of central vestibular pathology (4), present in 55% of patients (n = 185/334) (5-7) with AVS of central cause. Whether isolated acute truncal ataxia (ATA), without central oculomotor deficits, can occur in patients with acute vertigo has not to our knowledge been systematically evaluated. The aim of this study was to explore the frequency of truncal ataxia without concurrent nystagmus in a cross-section of patients admitted to the emergency department with acute vertigo.

# METHODS

## *Study Design and Settings*

A retrospective, observational, descriptive, and cross-sectional study of two groups of patients with acute vertigo attending the emergency departments (ED) of Santa Fe in Argentina between January 2018 and November 2021 (Group A) and the ED of University College London Hospitals in the United Kingdom between January 2022 and June 2022 (Group B). Group A and B comprised of 78 and 31 patients with vertigo attending the ED, respectively.

Ethical approvals were obtained from the UK Northwest - Greater Manchester South Research Ethics Committee (approval No. 21/NW/0015) and the Cullen Hospital (dependent on the Universidad Nacional del Litoral) in Argentina. All patients included in this study signed an informed consent.

*Participants and Study Procedure*

All patients included in both groups underwent general neurological and neuro-otological clinical bedside examination that included spontaneous nystagmus, with and without Frenzel glasses, saccades, pursuit, bedside head impulse test (video head impulse test in group B), vestibulo-ocular reflex (VOR) cancellation, subjective visual vertical (SVV) test Group A only), static and dynamic signs of the vestibulospinal reflex (deviation in the Bárány pointing test; Romberg's sign; Fukuda step test; tandem gait), and Dix-Hallpike and Roll positional tests. Truncal ataxia was measured by independent observers as grade 1, mild to moderate imbalance when walking independently; grade 2, severe imbalance on standing but unable to walk without support; grade 3, fall in an upright position (8). Headshaking was not routinely performed in either group.

All clinical assessments were performed in the ED by Neurologists within 24 hours of symptom onset. All patients underwent computerized tomography (CT) scan and/or magnetic resonance imaging of the brain with diffusion angiography, T1, T2 and FLAIR within 48 h of admission.

## RESULTS

In total, 78 participants were recruited in Argentina (Group A) and 31 patients from the UK (Group B). Seven cases from Group A and seven cases from Group B were excluded from the analysis because they did not fulfil the criteria for acute vertigo (abrupt onset and persistent sensation of self-motion when no self-motion is occurring or the sensation of distorted self-motion during an otherwise normal head movement). 71 patients from Group A and 24 from Group B were included in the final analysis. Group A age range was 30-80 years; mean 58 years, SD= 8.3 and in Group B was 25-83 years; mean= 57 SD= 16.5, not significantly different between the two groups ($p>0.1$). In Group A, of the 71 patients

with AVS, 43 were men and 28 women. In Group B, of the 24 patients with AVS, 7 were men and 17 women. Overall, 54% were male and 46% female.

Of 71 patients in Group A, 59 had AVS with nystagmus and 12 patients had ataxia without nystagmus. In Group B, of the 24 patients with AVS, 2 patients had ataxia without nystagmus.

In Group A, of the 59 patients with AVS with nystagmus, 24 had a cerebellar stroke, of whom 18 had a cerebellar stroke of the posterior inferior cerebellar artery (PICA), five had a cerebellar stroke of the anterior inferior cerebellar artery (AICA), and one patient had a stroke of the superior cerebellar artery (SCA, Figure 1). Twenty-eight patients presented with a diagnosis of a peripheral vestibular syndrome, of whom 19 patients presented a diagnosis of vestibular neuritis, seven patients a diagnosis of labyrinthine ischemia and two patients with Ramsay Hunt syndrome. Other causes were Wernicke's encephalopathy (n=3), multiple sclerosis (n=2), and medication-induced (anticonvulsant drugs, n=2).

In Group B, of the 22 patients with AVS with nystagmus, 19 patients had a central cause, of whom six had a cerebellar stroke, nine had vestibular migraine, one had a diagnosis of multiple sclerosis, and three had undefined ataxia syndromes, under investigation (e.g., spinocerebellar ataxia, episodic ataxia type 2). Of 22 patients with nystagmus, three patients presented a diagnosis of a peripheral vestibular disorder.

In Group A, of the 12 patients (out of 71) with AVS who presented to ED with ATA without nystagmus, five patients had a cerebellar stroke, three thalamic infarcts, two cerebral strokes in the territory of the right middle cerebral artery, one patient with multiple sclerosis and one patient with a cerebellar tumour (Figure 2). Of these 12 patients, five patients had grade 3 ataxia, and seven patients had grade 2 ataxia. Oculomotor findings (smooth pursuit, saccadic metrics, VOR cancelation) were normal in these 12 patients. There were no specific abnormal SVV patterns in these patients with ATA without nystagmus.

In Group B, the two patients with AVS presented to ED with ataxia without nystagmus had a cerebellar stroke (Figure 2). Of the two patients, one patient had grade 3 ataxia and

one patient had grade 2. Neither patient had abnormal eye movements (pursuit, saccadic metrics and VOR cancelation) at the bedside nor on oculography.

## DISCUSSION

We carried out a retrospective cross-sectional review of 95 patients with acute vertigo attending the ED at two centres (Argentina & UK) to determine the frequency of ATA in patients without evidence of nystagmus in the acute phase.

ATA presenting without nystagmus had a prevalence of 17% in Group A and 8% in Group B. There was a greater prevalence of central disorders in Group B, perhaps related to it being a tertiary University Neuroscience centre. Moreover, patients in Group B underwent instrumented oculography where detection of nystagmus may be superior to the bedside assessment. Indeed, in one patient in Group B with a proven stroke syndrome on imaging, subtle gaze-evoked nystagmus was only identified on oculography. Across 14 patients with ATA without nystagmus, seven patients had cerebellar stroke (three of these with involvement of the ACS, three involving the lateral posterior inferior cerebellar artery and one involving the paramedian midbrain), three thalamic infarcts, two cerebral strokes in the territory of the right middle cerebral artery, one patient with multiple sclerosis and one patient with a cerebellar tumour.

Four patients presented ataxia without nystagmus due to involvement of the lateral branch of the PICA, itself a branch of the vertebral artery. At the level of the upper part of the cerebellar tonsils the PICA descends through the lower vermis, dividing into two branches; the medial branch supplies the inferior vermis (nodulus, uvula, pyramids), inner part of the inferior semilunar lobule, and cerebellar tonsils (9). The lateral branch supplies the inferior lateral portion of the cerebellar hemisphere. Infarcts in the lateral territory of the PICA are rare and involve the anterolateral region of the caudal part of the cerebellar hemisphere. The most common symptoms include unsteadiness, gait ataxia, limb ataxia, and ipsilateral pulsion. There is no nystagmus, nor is dysarthria observed unless the brainstem is also involved (10), accounting for the presence of isolated ATA without nystagmus in our patients. PICA territory strokes affecting the medial branch

accounted for most acute central vestibular vascular syndromes (with nystagmus) in our cohort (n=19), characterized by vertigo, ipsilesional nystagmus and contralesional lateropulsion.

An infarction confined to the territory of the SCA may also present as a vestibulo-cerebellar syndrome with headache, gait ataxia, and vomiting. Vertigo and nystagmus are generally less prominent in patients with isolated SCA infarcts (11) that supplies the superior vermis and a large part of the cerebellar hemispheres in addition to the dentate nuclei, accounting for both limb and gait ataxia (12). In our series, 6/37 patients with cerebellar stroke had SCA involvement, of whom three presented with ataxia but without nystagmus.

Three patients with thalamic infarcts all had severe (grade 3) gait ataxia. Thalamic astasia describes postural instability, retropulsion, or lateropulsion due to involvement of the posterolateral thalamic area and central thalamus (13) that carry ipsilateral graviceptive signals via the vestibulothalamic tract.

Two patients with ATA without nystagmus had right hemisphere cerebral strokes, associated with unilateral visual neglect, and grade 2 gait ataxia (with associated subjective reports of unsteadiness at the onset of neurological motor symptoms). Whether such hemispheric bias relates to the suspected right hemispheric lateralisation of the vestibular network (14,15) or merely the small sample size remains to be seen. However, that truncal ataxia can be a presenting feature of cerebral stroke, in the absence of nystagmus, emphasises the importance of assessing gait in patients with acute neurological presentations, particularly as many such patients are brought into the emergency room on a stretcher, where the clinical examination is typically performed. Moreover, in such individuals, additional oculomotor assessment did no help identify central causes of vertigo when nystagmus was absent, even with the use of oculography.

## CONCLUSIONS

Although nystagmus was present acutely in 85% of patients with an acute vestibular syndrome, in the remaining 15% gait ataxia was a predominant neurological manifestation, without nystagmus. Our findings suggest that there is a subpopulation of

patients with acute vertigo in which the current standard approaches such as the HINTS examination that focus on oculomotor assessment may not be applicable, highlighting the need for a formal assessment of gait in this setting.

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Figure 1. Of the 81 patients with AVS with nystagmus in Group A and Group B, 30 had a cerebellar stroke, of whom 21 had a cerebellar stroke of the posterior inferior cerebellar artery, seven had a cerebellar stroke of the anterior inferior cerebellar artery, and two patients had a stroke of the superior cerebellar artery

Figure 2. Representative brain magnetic resonance imaging of patients in Group A and Group B with central acute vestibular syndromes presenting with gait ataxia and no evidence of nystagmus. SCA – superior cerebellar artery stroke; PICA – posterior inferior cerebellar artery stroke; MCA – middle cerebral artery stroke; MS – multiple sclerosis; Tumour – posterior cerebral fossa tumour.